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NEWS 7 MAR 03 MEDLINE file segment of TOXCENTER reloaded  
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available  
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=> s retigabine or d 23129 or 150812-12-7/rn

'RN' IS NOT A VALID FIELD CODE

'RN' IS NOT A VALID FIELD CODE

'RN' IS NOT A VALID FIELD CODE

L1 375 RETIGABINE OR D 23129 OR 150812-12-7/RN

=> s l1 and (pain or non-inflammatory or noninflammatory)

L2 47 L1 AND (PAIN OR NON-INFLAMMATORY OR NONINFLAMMATORY)

=> dup rem l2

PROCESSING COMPLETED FOR L2

L3 28 DUP REM L2 (19 DUPLICATES REMOVED)

=> focus

PROCESSING COMPLETED FOR L3

L4 28 FOCUS L3 1-

=> d ibib abs 1-28

L4 ANSWER 1 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:636213 CAPLUS

DOCUMENT NUMBER: 133:187979

TITLE: Use of **retigabine** for the treatment of  
**pain**

INVENTOR(S): Rundfeldt, Chris; Bartsch, Reni; Rostock, Angelika;  
Tober, Christine; Dost, Rita

PATENT ASSIGNEE(S): ASTA Medica Aktiengesellschaft, Germany

SOURCE: U.S., 5 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6117900	A	20000912	US 1999-406135	19990927
WO 2001022953	A2	20010405	WO 2000-EP9284	20000922
WO 2001022953	A3	20020523		
W:	AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE			
BR 2000014293	A	20020521	BR 2000-14293	20000922
EP 1223927	A2	20020724	EP 2000-969283	20000922
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY			

NZ 517616	A	20021220	NZ 2000-517616	20000922
JP 2003510273	T2	20030318	JP 2001-526165	20000922
EE 200200145	A	20030415	EE 2002-145	20000922
BG 106450	A	20020930	BG 2002-106450	20020227
HR 2002000234	A1	20030630	HR 2002-234	20020318
NO 2002001418	A	20020321	NO 2002-1418	20020321
ZA 2002002449	A	20030128	ZA 2002-2449	20020327

PRIORITY APPLN. INFO.:

US 1999-406135	A	19990927
WO 2000-EP9284	W	20000922

AB The invention relates to the use of 2-amino-4-(4-fluorobenzylamino)-1-ethoxycarbonylaminobenzene (**retigabine**), or a pharmaceutically utilizable salt thereof, for the prophylaxis and treatment of **pain**, e.g. neuropathic **pain**.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:65295 CAPLUS

DOCUMENT NUMBER: 139:46967

TITLE: The anticonvulsant **retigabine** attenuates nociceptive behaviours in rat models of persistent and neuropathic **pain**

AUTHOR(S): Blackburn-Munro, Gordon; Jensen, Bo Skaaning

CORPORATE SOURCE: Department of Pharmacology, NeuroSearch A/S, Ballerup, DK-2750, Den.

SOURCE: European Journal of Pharmacology (2003), 460(2-3), 109-116

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have tested for anti-nociceptive effects of the anticonvulsant KCNQ channel opener, N-(2-amino-4-(4-fluorobenzylamino)-phenyl)carbamic acid Et ester (**retigabine**), in rat models of exptl. **pain**. In the chronic constriction injury and spared nerve models of neuropathic **pain**, injection of **retigabine** (5 and 20 mg/kg, p.o.) significantly attenuated ( $P < 0.05$ ) mech. hypersensitivity in response to pin prick stimulation of the injured hindpaw. In contrast, **retigabine** had no effect on mech. hypersensitivity to von Frey stimulation of the injured hindpaw in either model. Cold sensitivity in response to Et chloride was only attenuated ( $P < 0.05$ ) in the chronic constriction injury model. In the formalin test, **retigabine** (20 mg/kg, p.o.) attenuated flinching behavior in the second phase compared with vehicle ( $P < 0.05$ ), and this effect was completely reversed by the KCNQ channel blocker 10,10-bis(4-pyridinylmethyl)-9(10H)-anthracenone (XE-991; 3 mg/kg, i.p.). Neither **retigabine** nor XE-991 administration affected the latency to respond to noxious thermal stimulation of the tail in control animals. These results suggest that **retigabine** may prove to be effective in the treatment of neuropathic **pain**.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:690613 CAPLUS

DOCUMENT NUMBER: 140:87016

TITLE: Lack of pharmacokinetic interaction between **retigabine** and phenobarbitone at steady-state in healthy subjects

AUTHOR(S): Ferron, Geraldine M.; Patat, Alain; Parks, Virginia; Rolan, Paul; Troy, Steven M.

CORPORATE SOURCE: Clinical Pharmacology Department, Wyeth Research, Collegeville, PA, USA

SOURCE: British Journal of Clinical Pharmacology (2003), 56(1), 39-45

CODEN: BCPHBM; ISSN: 0306-5251

PUBLISHER: Blackwell Publishing Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB To evaluate potential pharmacokinetic interactions between phenobarbitone and **retigabine**, a new antiepileptic drug. Fifteen healthy men received 200 mg of **retigabine** on day 1. On days 432, phenobarbitone 90 mg was administered at 22.00 h. On days 26-32, increasing doses of **retigabine** were given to achieve a final dose of 200 mg every 8 h on day 32. The pharmacokinetics of **retigabine** were determined on days 1 and 32, and those for phenobarbitone on days 25 and 31. After administration of a single 200 mg dose, **retigabine** was rapidly absorbed and eliminated with a mean terminal half-life of 6.7 h, a mean AUC of 3936 ng ml<sup>-1</sup> h and a mean apparent clearance of 0.761 h<sup>-1</sup> kg<sup>-1</sup>. Similar exposure to the partially active acetylated metabolite (AWD21-360) of **retigabine** was observed. After administration of phenobarbitone dosed to steady-state, the pharmacokinetics of **retigabine** at steady-state were similar (AUC of 4433 ng ml<sup>-1</sup> h and t<sub>1/2</sub> of 8.5 h) to those of **retigabine** alone. The AUC of phenobarbitone was 298 mg l<sup>-1</sup> h when administered alone and 311 mg ml<sup>-1</sup> h after **retigabine** administration. The geometric mean ratios and 90% confidence intervals of the AUC were 1.11 (0.97, 1.28) for **retigabine**, 1.01 (0.88, 1.06) for AWD21-360 and 1.04 (0.96, 1.11) for phenobarbitone. Individual and combined treatments were generally well tolerated. One subject was withdrawn from the study on day 10 due to severe abdominal pain. Headache was the most commonly reported adverse event. No clin. relevant changes were observed in the electrocardiograms, vital signs or laboratory measurements. There was no pharmacokinetic interaction between **retigabine** and phenobarbitone in healthy subjects. No dosage adjustment is likely to be necessary when **retigabine** and phenobarbitone are coadministered to patients.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:389379 CAPLUS

DOCUMENT NUMBER: 135:221181

TITLE: KCNQ4 channel activation by BMS-204352 and **retigabine**

AUTHOR(S): Schroder, R. L.; Jespersen, T.; Christophersen, P.; Strobaek, D.; Jensen, B. S.; Olesen, S.-P.

CORPORATE SOURCE: NeuroSearch A/S, Ballerup, DK 2750, Den.

SOURCE: Neuropharmacology (2001), 40(7), 888-898

CODEN: NEPHBW; ISSN: 0028-3908

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Activation of potassium channels generally reduces cellular excitability, making potassium channel openers potential drug candidates for the treatment of diseases related to hyperexcitability such as epilepsy, neuropathic pain, and neurodegeneration. Two compds., BMS-204352 and **retigabine**, presently in clin. trials for the treatment of stroke and epilepsy, resp., have been proposed to exert their protective action via an activation of potassium channels. Here we show that KCNQ4 channels, stably expressed in HEK293 cells, were activated by **retigabine** and BMS-204352 in a reversible and concentration-dependent manner in the concentration range 0.1-10 µM. Both compds. shifted the KCNQ4 channel activation curves towards more neg. potentials by about 10 mV. Further, the maximal current obtainable at large pos. voltages was also increased concentration-dependently by both compds. Finally, a pronounced slowing of the deactivation kinetics was induced in particular by BMS-204352. The M-current blocker linopirdine inhibited the baseline current, as well as the BMS-204352-induced activation of the KCNQ4

channels. KCNQ2, KCNQ2/Q3, and KCNQ3/Q4 channels were activated to a similar degree as KCNQ4 channels by 10  $\mu$ M of BMS-204352 and **retigabine**, resp. The compds. are, thus, likely to be general activators of M-like currents.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:283501 CAPLUS

TITLE: The anti-hyperalgesic activity of **retigabine** is mediated by KCNQ potassium channel activation

AUTHOR(S): Dost, R.; Rostock, A.; Rundfeldt, C.

CORPORATE SOURCE: elbion AG, Meissner Strasse 191, Radebeul, 01445, Germany

SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (2004), 369(4), 382-390

CODEN: NSAPCC; ISSN: 0028-1298

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Retigabine** (N-(2-amino-4-(4-fluorobenzylamino)-phenyl) carbamic acid Et ester) has a broad anticonvulsant spectrum and is currently in clin. development for epilepsy. The compound has an opening effect on neuronal KCNQ channels. At higher concns. an augmentation of gamma-aminobutyric acid (GABA) induced currents as well as a weak blocking effect on sodium and calcium currents were observed. The goal of this study was to characterize the activity of **retigabine** in models of acute and neuropathic **pain** and to investigate if the potassium channel opening effect of **retigabine** contributes to its activity. **Retigabine** was tested in mice and rats in the tail flick model of acute **pain** and in the nerve ligation model with tight ligation of the 5th spinal nerve (L5) using both thermal and tactile stimulation. While **retigabine** like gabapentin had almost no analgesic effect in mice it showed some analgesic effects in rats in the tail flick model. These effects could not be antagonized with linopirdine, a selective KCNQ potassium channel blocker, indicating a different mode of action for this activity. In L5-ligated rats **retigabine** significantly and dose-dependently elevated the **pain** threshold and prolonged the withdrawal latency after tactile and thermal stimulation, resp. In the L5 ligation model with thermal stimulation **retigabine** 10 mg/kg p.o. was as effective as 100 mg/kg gabapentin or 10 mg/kg tramadol. The L5 model with tactile stimulation was used to test the role of the KCNQ potassium channel opening effect of **retigabine**. If **retigabine** 10 mg/kg p.o. was administered alone it was as effective as tramadol 10 mg/kg p.o. in elevating the **pain** threshold. Linopirdine (1 and 3 mg/kg i.p.) had nearly no influence on neuropathic **pain** response. If we administered both **retigabine** and linopirdine the effect of **retigabine** was abolished or diminished depending on the dose of linopirdine used. In summary, **retigabine** is effective in predictive models for neuropathic **pain**. The activity is comparable to tramadol and is present at lower doses compared with gabapentin. Since the anti-allodynic effect can be inhibited by linopirdine we can conclude that the potassium channel opening properties of **retigabine** are critically involved in its ability to reduce neuropathic **pain** response.

L4 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:638248 CAPLUS

DOCUMENT NUMBER: 140:53256

TITLE: KCNQ/M currents in sensory neurons: Significance for **pain** therapy

AUTHOR(S): Passmore, Gayle M.; Selyanko, Alexander A.; Mistry, Mohini; Al-Qatari, Mona; Marsh, Stephen J.; Matthews,

CORPORATE SOURCE: Elizabeth A.; Dickenson, Anthony H.; Brown, Terry A.;  
 Burbidge, Stephen A.; Main, Martin; Brown, David A.  
 Department of Pharmacology, University College London,  
 London, WC1E 6BT, UK  
 SOURCE: Journal of Neuroscience (2003), 23(18), 7227-7236  
 CODEN: JNRSDS; ISSN: 0270-6474  
 PUBLISHER: Society for Neuroscience  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Neuronal hyperexcitability is a feature of epilepsy and both inflammatory and neuropathic **pain**. M currents [IK(M)] play a key role in regulating neuronal excitability, and mutations in neuronal KCNQ2/3 subunits, the mol. correlates of IK(M), have previously been linked to benign familial neonatal epilepsy. Here, we demonstrate that KCNQ/M channels are also present in nociceptive sensory systems. IK(M) was identified, on the basis of biophys. and pharmacol. properties, in cultured neurons isolated from dorsal root ganglia (DRGs) from 17-d-old rats. Currents were inhibited by the M-channel blockers linopirdine (IC<sub>50</sub>, 2.1 μM) and XE991 (IC<sub>50</sub>, 0.26 μM) and enhanced by **retigabine** (10 μM). The expression of neuronal KCNQ subunits in DRG neurons was confirmed using reverse transcription-PCR and single-cell PCR anal. and by immunofluorescence. **Retigabine**, applied to the dorsal spinal cord, inhibited C and Aδ fiber-mediated responses of dorsal horn neurons evoked by natural or elec. afferent stimulation and the progressive "windup" discharge with repetitive stimulation in normal rats and in rats subjected to spinal nerve ligation. **Retigabine** also inhibited responses to intrapaw application of carrageenan in a rat model of chronic **pain**; this was reversed by XE991. It is suggested that IK(M) plays a key role in controlling the excitability of nociceptors and may represent a novel analgesic target.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 28 USPATFULL on STN

ACCESSION NUMBER: 2002:283127 USPATFULL  
 TITLE: Modulatory binding site in potassium channels for screening and finding new active ingredients  
 INVENTOR(S): Rundfeldt, Chris, Coswig, GERMANY, FEDERAL REPUBLIC OF  
 Netzer, Rainer, Hamburg, GERMANY, FEDERAL REPUBLIC OF  
 PATENT ASSIGNEE(S): Arzneimittelwerk Dresden GmbH, Radebeul, GERMANY,  
 FEDERAL REPUBLIC OF (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6472165	B1	20021029
APPLICATION INFO.:	US 1999-368314		19990803 (9)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Guzo, David		
ASSISTANT EXAMINER:	Leffers, Jr., Gerald G.		
LEGAL REPRESENTATIVE:	Fulbright & Jaworski L.L.P.		
NUMBER OF CLAIMS:	11		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)		
LINE COUNT:	611		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A selective modulatory **retigabine** binding potassium channel receptor site containing subunits KCNQ2 and KCNQ3, and a method for directly selectively modulating that receptor site by administering **retigabine** to a cell preparation of the potassium channel.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 8 OF 28 USPATFULL on STN

ACCESSION NUMBER: 2003:238492 USPATFULL  
 TITLE: Cinnamide derivatives as KCNQ potassium channel modulators  
 INVENTOR(S): Wu, Yong-Jin, Madison, CT, UNITED STATES  
 Sun, Li-Quang, Glastonbury, CT, UNITED STATES  
 Chen, Jie, Madison, CT, UNITED STATES  
 He, Huan, Wallingford, CT, UNITED STATES  
 L'Heureux, Alexandre, Longueuil, CANADA  
 Dextraze, Pierre, Laprairie, CANADA  
 Daris, Jean-Paul, St. Hubert, CANADA  
 Kinney, Gene G., Collegeville, PA, UNITED STATES  
 Dworetzky, Steven I., Middlefield, CT, UNITED STATES  
 Hewawasam, Piyasena, Middletown, CT, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003166650	A1	20030904
APPLICATION INFO.:	US 2002-160582	A1	20020531 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-294815P	20010531 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000	
NUMBER OF CLAIMS:	28	
EXEMPLARY CLAIM:	1	
LINE COUNT:	4774	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB There is provided novel cinnamide derivatives of Formula I ##STR1##

wherein R is C.sub.1-4 alkyl or trifluoromethyl; R.sup.1 is selected from the group consisting of pyridinyl, quinolinyl, thienyl, furanyl, 1,4-benzodioxanyl, 1,3-benzodioxolyl, chromanyl, indanyl, biphenyl, phenyl and substituted phenyl in which said substituted phenyl is substituted with one or two substituents each independently selected from the group consisting of halogen, C.sub.1-4 alkyl, C.sub.1-4 alkoxy, trifluoromethyl, trifluoromethoxy and nitro; R.sup.2 and R.sup.3 are each independently selected from the group consisting of hydrogen, C.sub.1-4 alkyl, and halogen; R.sup.4 is selected from the group consisting of di(C.sub.1-4 alkyl)amino, trifluoromethoxy and optionally substituted morpholin-4-yl, pyridinyl, pyrimidinyl, piperazinyl, and pyrazinyl with one or two substituents in which said substituent is independently selected from the group consisting of C.sub.1-4 alkyl, aminomethyl, hydroxymethyl, chloro or fluoro; R.sup.5 is hydrogen, chloro or fluoro; or R.sup.4 and R.sup.5 taken together are --CH.dbd.CH--CH.dbd.CH-- or --X(CH.sub.2).sub.mY-- in which X and Y are each independently selected from the group consisting of CH.sub.2, (CH.sub.2).sub.nN(R.sup.9)-- and O, wherein m is 1 or 2; n is 0 or 1; and R.sup.6, R.sup.7, and R.sup.8 are each independently selected from hydrogen, chloro and fluoro; and R.sup.9 is selected from the group consisting of hydrogen, C.sub.1-4 alkyl, hydroxyethyl, C.sub.1-4 alkoxyethyl, cyclopropylmethyl, --CO.sub.2(C.sub.1-4alkyl), and --CH.sub.2CH.sub.2NR.sup.10R.sup.11 in which R.sup.10 and R.sup.11 are each independently hydrogen or C.sub.1-4 alkyl, which are openers of the KCNQ potassium channels and are useful in the treatment of disorders which are responsive to the opening of the KCNQ potassium channels.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 9 OF 28 USPATFULL on STN

ACCESSION NUMBER: 2002:323226 USPATFULL  
 TITLE: Methods for treating hyperactive gastric motility

INVENTOR(S): Argentieri, Thomas M., Yardley, PA, UNITED STATES  
PATENT ASSIGNEE(S): Wyeth, Madison, NJ (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002183395	A1	20021205
APPLICATION INFO.:	US 2002-114148	A1	20020402 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-281471P	20010404 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	George M. Tarnowski, 5 Giralda Farms, Madison, NJ, 07940	
NUMBER OF CLAIMS:	23	
EXEMPLARY CLAIM:	1	
LINE COUNT:	719	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides methods and pharmaceutical compositions for treating, inhibiting or preventing hyperactive gastric motility in a mammal utilizing agonists of KCNQ potassium channels, including KCNQ2, KCNQ3, KCNQ4 and KCNQ5 potassium channels, alone or in combination. The hyperactive gastric motility may be associated with maladies including, colitis, irritable bowel syndrome and Crohn's disease. Compounds useful in these methods include the 1,2,4-triamino-benzene derivatives described in U.S. Pat. Number 5,384,330 (Dieter et al.) and the substituted 3-phenyl oxindole compounds described in U.S. Pat. Number 5,565,483 (Hewawasam et al.). Among the preferred compounds of this invention is N-[2-amino-4-(4-fluorobenzylamino)-phenyl]carbamic acid ethyl ester, also referred to as **retigabine**.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 10 OF 28 USPATFULL on STN  
ACCESSION NUMBER: 2002:236079 USPATFULL  
TITLE: Modulators of KCNQ potassium channels and use thereof in treating migraine and mechanistically related diseases  
INVENTOR(S): Dworetzky, Steven I., Middlefield, CT, UNITED STATES  
Gribkoff, Valentin K., Wallingford, CT, UNITED STATES  
Kinney, Gene G., Collegeville, PA, UNITED STATES  
Hewawasam, Piyasena, Middletown, CT, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002128277	A1	20020912
APPLICATION INFO.:	US 2002-75703	A1	20020214 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-269967P	20010220 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Stephen B. Davis, BRISTOL-MYERS SQUIBB COMPANY, Patent Department, P. O. Box 4000, Princeton, NJ, 08543-4000	
NUMBER OF CLAIMS:	16	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	7 Drawing Page(s)	
LINE COUNT:	1482	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds which function as modulators, particularly, openers, of human KCNQ potassium channel proteins or polypeptides, particularly, central nervous system (CNS)-located KCNQ potassium channels, and

heteromultimers thereof, and their use in the treatment of migraine are provided by the present invention. One novel type of potassium channel polypeptide openers provided by the present invention is the fluorooxindole compounds, described for the first time as therapeutics for the treatment of migraine by preventing the asynchronous firing of neurons. Other KCNQ potassium channel opener compounds that are also useful in the treatments of the invention include 2,4-disubstituted pyrimidine-5-carboxamide derivatives. One or more of the compounds according to the present invention may be utilized alone, in combination, or in conjunction with other treatment modalities for reducing, ameliorating and/or alleviating migraine or diseases similar to, or mechanistically related to, migraine, e.g., cluster headache.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 11 OF 28 USPATFULL on STN

ACCESSION NUMBER: 2004:39407 USPATFULL  
TITLE: Methods for treating hyperactive gastric motility  
INVENTOR(S): Argentieri, Thomas M., Yardley, PA, UNITED STATES  
PATENT ASSIGNEE(S): Wyeth, Madison, NJ, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004029949	A1	20040212
APPLICATION INFO.:	US 2003-635081	A1	20030806 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2002-114148, filed on 2 Apr 2002, ABANDONED		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-281471P	20010404 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	WYETH, PATENT LAW GROUP, FIVE GIRALDA FARMS, MADISON, NJ, 07940	
NUMBER OF CLAIMS:	6	
EXEMPLARY CLAIM:	1	
LINE COUNT:	629	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides methods and pharmaceutical compositions for treating, inhibiting or preventing hyperactive gastric motility in a mammal utilizing agonists of KCNQ potassium channels, including KCNQ2, KCNQ3, KCNQ4 and KCNQ5 potassium channels, alone or in combination. The hyperactive gastric motility may be associated with maladies including, colitis, irritable bowel syndrome and Crohn's disease. Compounds useful in these methods include the 1,2,4-triamino-benzene derivatives described in U.S. Pat. Number 5,384,330 (Dieter et al.) and the substituted 3-phenyl oxindole compounds described in U.S. Pat. Number 5,565,483 (Hewawasam et al.).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 12 OF 28 USPATFULL on STN

ACCESSION NUMBER: 2003:258454 USPATFULL  
TITLE: Use of 3-substituted oxindole derivatives as kcnq potassium channel modulators  
INVENTOR(S): Jensen, Bo Skaaning, Ballerup, DENMARK  
Schroder, Rikke, frederiksberg, DENMARK  
Strobaek, Dorte, Ballerup, DENMARK  
Olesen, Soren Peter, Ballerup, DENMARK

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003181507	A1	20030925

APPLICATION INFO.: US 2003-312123 A1 20030224 (10)  
WO 2001-DK412 20010614

	NUMBER	DATE
PRIORITY INFORMATION:	DK 2000-1022	20000629
	DK 2001-394	20010308
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	BIRCH STEWART KOLASCH & BIRCH, PO BOX 747, FALLS CHURCH, VA, 22040-0747	
NUMBER OF CLAIMS:	9	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	4 Drawing Page(s)	
LINE COUNT:	762	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a novel method of treating of **pain** or anxiety, using compounds that modulate KCNQ potassium channels and currents. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:933608 CAPLUS  
TITLE: The therapeutic potential of neuronal KCNQ channel modulators  
AUTHOR(S): Gribkoff, Valentin K.  
CORPORATE SOURCE: Department 401, Neuroscience Drug Discovery, Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, CT, 06492, USA  
SOURCE: Expert Opinion on Therapeutic Targets (2003), 7(6), 737-748  
CODEN: EOTTAO; ISSN: 1472-8222  
PUBLISHER: Ashley Publications Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Neuronal KCNQ (Kv7) channels (KCNQ2 - 5 or Kv7.2 - 7.5, disclosed to date) were discovered by virtue of their homol. with a known cardiac channel involved in long QT syndrome (KvLQT or KCNQ1, Kv7.1) and first disclosed in 1998. The involvement of KCNQ2 (Kv7.2) and KCNQ3 (Kv7.3) in a benign idiopathic neonatal epilepsy, KCNQ4 (Kv7.4) in a form of congenital deafness, and the discovery that neuronal KCNQ heteromultimers were among the mol. substrates of M-channels, resulted in a high level of interest for potential drug development strategies. A number of small-mol. modulators were quickly identified, including openers or activators such as the antiepileptic drug candidate **retigabine** and the structurally-related analgesic drug flupirtine (Katadolon Asta Medica), and a group of KCNQ channel inhibitors/blockers originally developed for cognition enhancement. All of these data have suggested a rich target profile for modulators of neuronal KCNQ channels, including a variety of neuronal hyperexcitability disorders and conditions for openers, such as the epilepsies, acute **pain**, neuropathic **pain**, migraine **pain** and some neurodegenerative and psychiatric disorders. KCNQ blockers could likewise have utility in disorders characterised by neuronal hypoactivity, including cognition enhancement and perhaps disorders of mood. Emerging patent literature suggests significant interest in neuronal KCNQ modulation in the pharmaceutical industry and significant chemical diversity concerning KCNQ modulation.

REFERENCE COUNT: 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 28 USPATFULL on STN

ACCESSION NUMBER: 2002:34456 USPATFULL

TITLE: Methods for modulating bladder function  
INVENTOR(S): Argentieri, Thomas Michael, Yardley, PA, United States  
Sheldon, Jeffrey Howard, Trappe, PA, United States  
Bowlby, Mark R., Richboro, PA, United States  
PATENT ASSIGNEE(S): American Home Products Corporation, Madison, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6348486	B1	20020219
APPLICATION INFO.:	US 2001-977828		20011015 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-241078P	20001017 (60)
	US 2001-281428P	20010404 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Henley, III, Raymond	
LEGAL REPRESENTATIVE:	Eck, Steven R.	
NUMBER OF CLAIMS:	32	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)	
LINE COUNT:	651	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides methods and pharmaceutical compositions for maintaining bladder control or treating urinary incontinence in a mammal utilizing agonists of KCNQ potassium channels, including KCNQ2, KCNQ3, KCNQ4 and KCNQ5 potassium channels, alone or in combination. Compounds useful in these methods include the 1,2,4-triamino-benzene derivatives described in U.S. Pat. Number 5,384,330 (Dieter et al.) and the substituted 3-phenyl oxindole compounds described in U.S. Pat. Number 5,565,483 (Hewawasam et al.). Among the preferred compounds of this invention is N-[2-amino-4-(4-fluorobenzylamino)-phenyl]carbamic acid ethyl ester, also referred to as **retigabine**.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 15 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2002330231 EMBASE  
TITLE: New pharmacological strategies for **pain** relief.  
AUTHOR: Gillen C.; Maul C.  
CORPORATE SOURCE: Dr. C. Gillen, Molecular Pharmacology, Gruenenthal GmbH, Zieglerstr. 6, 52078 Aachen, Germany.  
Clemens.gillen@grunenthal.edu  
SOURCE: Expert Review of Neurotherapeutics, (2002) 2/5 (691-702).  
Refs: 67  
ISSN: 1473-7175 CODEN: ERN~~X~~AR  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 008 Neurology and Neurosurgery  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Persistent or chronic **pain** is the primary reason people seek medical advice. Despite major advances in the neurobiology of **pain**, many patients with chronic **pain** still remain insufficiently relieved. The urgent medical need for novel and safe analgesics with high efficacy has led to intense research for new targets and we want to give a comprehensive overview on the current strategies in molecular **pain** research. The recently-discovered or re-evaluated targets that yielded

compounds in clinical development will be summarized. In addition, we want to present emerging molecular strategies for **pain** relief, along with a mechanism-based classification of **pain** as the underlying concept for future diagnosis and therapy of chronic **pain**.

L4 ANSWER 16 OF 28 USPATFULL on STN

ACCESSION NUMBER: 2004:7342 USPATFULL  
TITLE: Proteins and nucleic acids encoding same  
INVENTOR(S): Guo, Xiaojia (Sasha), Branford, CT, UNITED STATES  
Li, Li, Branford, CT, UNITED STATES  
Patturajan, Meera, Branford, CT, UNITED STATES  
Shimkets, Richard A., Guilford, CT, UNITED STATES  
Casman, Stacie J., North Haven, CT, UNITED STATES  
Malyankar, Uriel M., Branford, CT, UNITED STATES  
Tchernev, Velizar T., Branford, CT, UNITED STATES  
Vernet, Corine A., North Branford, CT, UNITED STATES  
Spytek, Kimberly A., New Haven, CT, UNITED STATES  
Shenoy, Suresh G., Branford, CT, UNITED STATES  
Alsobrook, John P., II, Madison, CT, UNITED STATES  
Edinger, Schlomit, New Haven, CT, UNITED STATES  
Peyman, John A., New Haven, CT, UNITED STATES  
Stone, David J., Guilford, CT, UNITED STATES  
Ellerman, Karen, Branford, CT, UNITED STATES  
Gangolli, Esha A., Madison, CT, UNITED STATES  
Boldog, Ferenc L., North Haven, CT, UNITED STATES  
Colman, Steven D., Guilford, CT, UNITED STATES  
Eisen, Andrew, Rockville, MD, UNITED STATES  
Liu, Xiaohong, Lexington, MA, UNITED STATES  
Padigaru, Muralidhara, Branford, CT, UNITED STATES  
Spaderna, Steven K., Berlin, CT, UNITED STATES  
Zerhusen, Bryan D., Branford, CT, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004005576	A1	20040108
APPLICATION INFO.:	US 2002-231913	A1	20020830 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2001-10680, filed on 6 Dec 2001, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-251660P	20001206 (60)
	US 2001-260326P	20010108 (60)
	US 2001-318712P	20010912 (60)
	US 2000-255029P	20001212 (60)
	US 2001-263800P	20010124 (60)
	US 2001-286183P	20010424 (60)
	US 2001-269942P	20010220 (60)
	US 2001-313627P	20010820 (60)

DOCUMENT TYPE: Utility  
FILE SEGMENT: APPLICATION  
LEGAL REPRESENTATIVE: MINTZ, LEVIN, COHN, FERRIS, GLOVSKY, AND POPEO, P.C.,  
ONE FINANCIAL CENTER, BOSTON, MA, 02111

NUMBER OF CLAIMS: 41  
EXEMPLARY CLAIM: 1  
LINE COUNT: 17887

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are polypeptides and nucleic acids encoding same. Also disclosed are vectors, host cells, antibodies and recombinant methods for producing the polypeptides and polynucleotides, as well as methods for using same.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 17 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
 ACCESSION NUMBER: 2004:134964 BIOSIS  
 DOCUMENT NUMBER: PREV200400137120  
 TITLE: **Retigabine** hyperpolarises rat dorsal root ganglion cells and reduces excitability by activation of KCNQ channels.  
 AUTHOR(S): Herrik, Kjartan Frisch [Reprint Author]; Jensen, Henrik Sindal [Reprint Author]; Stroebaek, Dorte [Reprint Author]; Jensen, Bo Skaaning [Reprint Author]; Christophersen, Palle [Reprint Author]  
 CORPORATE SOURCE: NeuroSearch, Ballerup, Denmark  
 SOURCE: Biophysical Journal, (January 2004) Vol. 86, No. 1, pp. 532a. print.  
 Meeting Info.: 48th Annual Meeting of the Biophysical Society. Baltimore, MD, USA. February 14-18, 2004. Biophysical Society.  
 ISSN: 0006-3495 (ISSN print).  
 DOCUMENT TYPE: Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 10 Mar 2004  
 Last Updated on STN: 10 Mar 2004

AB In neuropathic **pain**, dorsal root ganglion (DRG) neurons may shift activity pattern from the normally silent phenotype driven by sensory inputs to a spontaneous active type responsible for ectopic input to **pain** centers in the CNS. Increasing the resting K<sup>+</sup>-conductance in DRG could dampen such activity. KCNQ2-5 channels are voltage-activated potassium channels active below the action potential threshold and potentially important for excitability regulation. Furthermore, the KCNQ channel activator, **retigabine**, shows effect in rat models of chronic **pain**. Using whole-cell patch clamp and real-time RT-PCR we investigated whether expression and function of KCNQ channels in isolated DRG from normal embryonic (eDRG) and adult rats (aDRG) may, at least partly, explain the analgesic effect of **retigabine**. Spontaneously active, cultured DRG cells firing APs at a constant rate were rarely observed (1 of 202 eDRG) although more frequently in aDRGs (5 of 45 cells). **Retigabine** (10 uM) reversibly silenced these cells by hyperpolarization. Likewise, current-evoked single APs were ameliorated. The effect was quantified by concentration-response experiments in the low uM concentration range and both capsaicin sensitive as well as insensitive cells responded to **retigabine**. XE-991 (30 uM), a selective KCNQ blocker, completely reversed the effect, as did TEA in the concentration range of 1-10 mM. In voltage-clamp, **retigabine** left-shifted the zero-current potential and increased the zero-current conductance, indicating augmented potassium conductance. In some cells **retigabine** clearly activated currents with M-channel characteristics. Real time RT-PCR studies with acutely dissociated DRG showed most prominent mRNA signal from KCNQ2, but all subtypes were detected. KCNQ2 and KCNQ3 were downregulated in adult rat DRG leaving KCNQ4 and KCNQ5 as the most frequent. These studies indicate expression and functional importance of KCNQ channels in rat DRG verifying KCNQ-channels as important **pain** targets.

L4 ANSWER 18 OF 28 USPATFULL on STN  
 ACCESSION NUMBER: 2002:206680 USPATFULL  
 TITLE: Methods of treating anxiety disorders  
 INVENTOR(S): Bowlby, Mark R., Richboro, PA, UNITED STATES  
 Rosenzweig-Lipson, Sharon J., East Brunswick, NJ, UNITED STATES  
 PATENT ASSIGNEE(S): American Home Products Corporation, Madison, NJ (U.S. corporation)

NUMBER	KIND	DATE
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PATENT INFORMATION:	US 2002111379	A1	20020815
	US 6589986	B2	20030708
APPLICATION INFO.:	US 2001-22579	A1	20011217 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-256834P	20001220 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	WYETH, FIVE GIRALDA FARMS, MADISON, NJ, 07940	
NUMBER OF CLAIMS:	7	
EXEMPLARY CLAIM:	1	
LINE COUNT:	336	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides methods for treating, preventing or inhibiting anxiety, anxiety-related conditions and phobias in a mammal using compounds of the formula: ##STR1##

wherein: R.sub.1 is H, alkyl, alkanoyl or the radical Ar; R.sub.2 is H or alkyl; R.sub.3 is alkoxy, NH.sub.2, alkylamino, dialkylamino, amino substituted by the radical Ar, alkyl, alkenyl, alkynyl, or the radicals Ar or ArO--; R.sub.4 is H, alkyl or the radical Ar; R.sub.5 is H or alkyl or the radical Ar; or a pharmaceutically acceptable salt or ester form thereof; Ar is an optionally substituted phenyl radical; and n is 0 or 1, or a pharmaceutically acceptable salt or ester form thereof, with the methods particularly including the use of N-[2-amino-4-(4-fluorobenzylamino)-phenyl]carbamic acid ethyl ester, also known as **retigabine**.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 19 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2004147403 EMBASE  
 TITLE: Neuropathic **Pain**: Drug Targets for Current and Future Interventions.  
 AUTHOR: Smith P.A.  
 CORPORATE SOURCE: Dr. P.A. Smith, Department of Pharmacology, University of Alberta, 9.75 Medical Sciences Building, Edmonton, Alta. T6G 2H7, Canada. peter.a.smith@ualberta.ca  
 SOURCE: Drug News and Perspectives, (2004) 17/1 (5-17).  
 Refs: 188  
 ISSN: 0214-0934 CODEN: DNPEED  
 COUNTRY: Spain  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 008 Neurology and Neurosurgery  
 030 Pharmacology  
 037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

AB Nociceptive **pain** alerts the body to potential or actual tissue damage. By contrast, neuropathic **pain**, which results from injury or damage to the nervous system, persists long after all signs of the original injury have disappeared. This type of maladaptive **pain** presents a significant clinical problem, as it responds poorly or unpredictably to classical analgesics. There is also no single, uniformly well-tolerated drug that is reliably helpful. Current understanding of the etiology of neuropathic **pain** reveals seven potential targets for therapeutic intervention. These are: 1) ectopic activity in damaged peripheral nerves; 2) increased excitability in spinal dorsal horn neurons; 3) restoration or augmentation of GABAergic inhibition in the dorsal horn; 4) supraspinal and affective mechanisms; 5) alterations in the sympathetic nervous system; 6) spinal peptidergic mechanisms; and 7)

spinal excitatory amino acid receptors. Current therapeutic approaches, using drugs such as gabapentin, anticonvulsants, ketamine or methadone, and potential new approaches are discussed in the context of these seven drug targets. .COPYRGT. 2004 Prous Science. All rights reserved.

L4 ANSWER 20 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2002148550 EMBASE  
TITLE: Anticonvulsants for the management of **pain**.  
AUTHOR: Chong M.S.; Smith T.E.  
CORPORATE SOURCE: M.S. Chong, Department of Neurology, King's College Hospital, Mapother House, De Crespigny Park, London SE5 9AZ, United Kingdom. mschong@doctors.org.uk  
SOURCE: Pain Reviews, (2000) 7/3-4 (129-149).  
Refs: 214  
ISSN: 0968-1302 CODEN: PAREFV  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 008 Neurology and Neurosurgery  
024 Anesthesiology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
050 Epilepsy  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB The development of anticonvulsant drugs is an example of where advances in basic neuroscience have improved patient care. Potential benefits also spill over to nonepileptic patients, especially those with chronic **pain**. It is increasingly recognized that there are many similarities between the molecular pathophysiology of epileptogenesis and that of chronic **pain**. Anticonvulsant drugs are now used extensively for treating neuropathic and non-neuropathic **pain** syndromes. This article summarizes the presumed modes of action of commonly used anticonvulsant drugs and points out where they may be important for treating **pain**. The clinical evidence for their efficacy is examined. In addition, some anticonvulsant drugs that are under development are assessed and those that may be effective for treating **pain** are highlighted.

L4 ANSWER 21 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2003332017 EMBASE  
TITLE: Adjunct agents in **pain** management:  
Anticonvulsants in the management of **pain**.  
AUTHOR: Khan T.  
CORPORATE SOURCE: T. Khan, Department of Anesthesiology, Emory University, Atlanta, GA, United States  
SOURCE: Progress in Anesthesiology, (2003) 17/12 (183-202).  
Refs: 316  
ISSN: 0891-5784 CODEN: PRANDM  
COUNTRY: United States  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 008 Neurology and Neurosurgery  
024 Anesthesiology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: English

L4 ANSWER 22 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2003:326545 BIOSIS  
DOCUMENT NUMBER: PREV200300326545  
TITLE: FLUPIRTINE A POSITIVE MODULATOR OF HETEROMERIC KCNQ2/Q3 CHANNELS.  
AUTHOR(S): Ilyin, V. I. [Reprint Author]; Carlin, K. P. [Reprint

Author]; Hodges, D. D. [Reprint Author]; Robledo, S.  
[Reprint Author]; Woodward, R. M. [Reprint Author]  
CORPORATE SOURCE: Discovery Research, Purdue Pharma L P, Cranbury, NJ, USA  
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary  
Planner, (2002) Vol. 2002, pp. Abstract No. 758.10.  
<http://sfn.scholarone.com.cd-rom>.  
Meeting Info.: 32nd Annual Meeting of the Society for  
Neuroscience. Orlando, Florida, USA. November 02-07, 2002.  
Society for Neuroscience.  
DOCUMENT TYPE: Conference; (Meeting)  
Conference; (Meeting Poster)  
Conference; Abstract; (Meeting Abstract)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 16 Jul 2003  
Last Updated on STN: 16 Jul 2003

AB KCNQ genes encode a group of potassium channels widely expressed in excitable tissues. Recent reports indicate that KCNQ2/3 heteromeric channels may underlie the native M-current in the CNS. KCNQ channels display slow activation and deactivation and little if any inactivation. Because a portion of these channels are open at normal resting membrane potentials, these channels suppress spike generation, making them potential targets for modulating activity in **pain** pathways. Flupirtine is a marketed analgesic whose mechanism of action is poorly defined. Because of the structural similarities between flupirtine and known KCNQ channel modulators we sought to determine if flupirtines analgesic activity could be mediated by KCNQ channels. We tested flupirtine side-by-side with **retigabine**, a known positive modulator of KCNQ channels. Using whole-cell patch clamp recordings from HEK-293 cells transiently transfected with KCNQ2/KCNQ3 constructs we determined that flupirtine is a positive modulator of KCNQ channels with a mechanism of action similar to that of **retigabine**. Application of flupirtine (10 uM) leads to an increase in current amplitude, a hyperpolarizing shift in the activation curve (-16+3mV) and an approximately 2 fold slowing of the deactivation kinetics. Flupirtine was a less potent modulator of KCNQ2/KCNQ3 channels than **retigabine**. In the rat Chung model of neuropathic **pain** flupirtine was equipotent to **retigabine** in reducing tactile allodynia but was less efficacious. We conclude that flupirtines effectiveness as an analgesic may be due, at least in part, to the positive modulation of KCNQ channels.

L4 ANSWER 23 OF 28 USPATFULL on STN  
ACCESSION NUMBER: 2002:338226 USPATFULL  
TITLE: Bisarylamine as potassium channel openers  
INVENTOR(S): Andrew McNaughton-Smith, Grant, Morrisville, NC, UNITED STATES  
Salvatore Amato, George, Cary, NC, UNITED STATES  
PATENT ASSIGNEE(S): ICAgen, Inc., Durham, NC, 27703 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002193597	A1	20021219
	US 6593349	B2	20030715
APPLICATION INFO.:	US 2002-95617	A1	20020311 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-277329P	20010319 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834	
NUMBER OF CLAIMS:	65	
EXEMPLARY CLAIM:	1	

NUMBER OF DRAWINGS: 11 Drawing Page(s)

LINE COUNT: 1810

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds, compositions and methods are provided which are useful in the treatment of diseases through the modulation of potassium ion flux through voltage-dependent potassium channels. More particularly, the invention provides bisarylamines, compositions and methods that are useful in the treatment of central or peripheral nervous system disorders (e.g., migraine, ataxia, Parkinson's disease, bipolar disorders, trigeminal neuralgia, spasticity, mood disorders, brain tumors, psychotic disorders, myokymia, seizures, epilepsy, hearing and vision loss, Alzheimer's disease, age-related memory loss, learning deficiencies, anxiety and motor neuron diseases) and as neuroprotective agents (e.g., to prevent stroke and the like) by opening potassium channels associated with the onset or recurrence of the indicated conditions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:213191 CAPLUS

TITLE: Pharmacological characterization of acid-induced muscle allodynia in rats

AUTHOR(S): Nielsen, Alexander Norup; Mathiesen, Claus; Blackburn-Munro, Gordon

CORPORATE SOURCE: NeuroSearch A/S, Department of Pharmacology, Ballerup, DK-2750, Den.

SOURCE: European Journal of Pharmacology (2004), 487(1-3), 93-103

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Previous studies have shown that repeated injections of acidic saline, given into the lateral gastrocnemius muscle of rats, results in a bilateral reduction in withdrawal threshold to tactile stimulation of the hindpaws. We have now characterised this model of musculoskeletal **pain** pharmacol., by evaluating the antinociceptive effects of various analgesics after systemic administration. The  $\mu$ -opioid receptor agonist morphine (3 and 6 mg/kg) produced a particularly prolonged antiallodynic effect. The glutamate receptor antagonists ([8-methyl-5-(4-(N,N-dimethylsulfamoyl)phenyl)-6,7,8,9,-tetrahydro-1H-pyrrolo[3,2-h]-iso-quinoline-2,3-dione-3-O-(4-hydroxybutyric acid-2-yl)oxime] NS1209 and ketamine (6 and 15 mg/kg, resp.), the KCNQ K<sup>+</sup> channel openers **retigabine** and flupirtine (10 and 20 mg/kg, resp.) and the Na<sup>+</sup> channel blocker mexiletine (37.5 mg/kg) also significantly increased paw withdrawal threshold, although to a lesser degree than morphine. In contrast, the anticonvulsant lamotrigine (30 mg/kg), the cyclooxygenase-2 inhibitor carprofen (15 mg/kg) and the benzodiazepine diazepam (3 mg/kg) were ineffective. All antinociceptive effects were observed at nonataxic doses as determined by the rotarod test.

These

results suggest that in this model, muscle-mediated **pain** can be alleviated by various analgesics with differing mechanisms of action, and that once established ongoing inflammation does not appear to contribute to this process.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003040622 EMBASE

TITLE: Therapeutic potential of potassium channel modulators for CNS disorders.

AUTHOR: Clark A.G.; Booth S.E.; Morrow J.A.  
 CORPORATE SOURCE: A.G. Clark, Lead Discovery Pharmacology, Organon  
 Laboratories Ltd., Newhouse, Lanarkshire ML1 5SH, United  
 Kingdom. a.clark@organon.co.uk  
 SOURCE: Expert Opinion on Therapeutic Patents, (1 Jan 2003) 13/1  
 (23-32).  
 Refs: 49  
 ISSN: 1354-3776 CODEN: EOTPEG  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 008 Neurology and Neurosurgery  
 030 Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

AB Potassium (K(+)) channels play a pivotal role in the CNS, controlling cell  
 excitability thereby raising their therapeutic application. In realisation  
 of the utility of K(+) channels, many pharmaceutical companies have  
 developed a plethora of antagonists and openers for a range of disorders,  
 including stroke, epilepsy, pain and cognition. The most  
 promising targets, including BK(Ca), SK(Ca) and KCNQ channels, will be  
 reviewed in this article. The focus will be upon the most recent K(+)  
 channel modulator patents for CNS disorders and future developments of  
 drugs for the treatment of CNS disorders.

L4 ANSWER 26 OF 28 USPATFULL on STN

ACCESSION NUMBER: 2002:323169 USPATFULL  
 TITLE: 2, 4-disubstituted pyrimidine-5-carboxamide derivatives  
 as KCNQ potassium channel modulators  
 INVENTOR(S): Hewawasam, Piyasena, Middletown, CT, UNITED STATES  
 Dodd, Dharmpal S., Princeton, NJ, UNITED STATES  
 Weaver, Charles D., Wallingford, CT, UNITED STATES  
 Dextraze, Pierre, Laprairie, CANADA  
 Gribkoff, Valentin K., Wallingford, CT, UNITED STATES  
 Kinney, Gene G., Collegeville, PA, UNITED STATES  
 Dworetzky, Steven I., Middlefield, CT, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002183335	A1	20021205
APPLICATION INFO.:	US 2002-75521	A1	20020214 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-269800P	20010220 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000	
NUMBER OF CLAIMS:	6	
EXEMPLARY CLAIM:	1	
LINE COUNT:	1346	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB There is provided a method of treatment for disorders responsive to the  
 modulation of KCNQ potassium channels by administering to a mammal in  
 need thereof a therapeutically effective amount of a 2,4-disubstituted  
 pyrimidine-5-carboxamide derivative of the Formula I ##STR1##

wherein R.sup.1, R.sup.2, R.sup.3, R.sup.4 and R.sup.5 are as defined  
 below. The present invention also provides pharmaceutical compositions  
 comprising openers or activators of the KCNQ potassium channels and  
 especially to the method of treatment of disorders sensitive to KCNQ  
 potassium channel opening activity such as migraine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 27 OF 28 USPATFULL on STN

ACCESSION NUMBER: 2002:276113 USPATFULL  
TITLE: Fluoro oxindole derivatives as modulators of KCNQ  
potassium channels  
INVENTOR(S): Hewawasam, Piyasena, Middletown, CT, United States  
Dextraze, Pierre, Laprairie, CANADA  
Gribkoff, Valentin K., Wallingford, CT, United States  
Kinney, Gene G., Collegeville, CT, United States  
Dworetzky, Steven I., Middlefield, CT, United States  
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, Princeton, NJ, United  
States (U.S. corporation)

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PRIMARY EXAMINER:	Lambkin, Deborah C.	
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LEGAL REPRESENTATIVE:	Algieri, Aldo A.	
NUMBER OF CLAIMS:	12	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)	
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB There is provided novel 3-fluoro-3-phenyl oxindole derivatives of  
Formula I ##STR1##

wherein

R.sup.1, R.sup.2, R.sup.3 and R.sup.4 each are independently hydrogen,  
C.sub.1-4 alkyl, halogen, fluoromethyl, trifluoromethyl, phenyl,  
4-methylphenyl or 4-trifluoromethylphenyl;

R.sup.5 is C.sub.1-6 alkyl optionally substituted with one to three same  
or different groups selected from fluoro and chloro, provided R.sup.5 is  
not C.sub.1-6 alkyl when Y is O;

Y is O or S; and

R.sup.6 and R.sup.7 each are independently hydrogen, chloro, bromo or  
trifluoromethyl;

which are openers of the KCNQ potassium channels and are useful in the  
treatment of disorders which are responsive to the opening of the KCNQ  
potassium channels.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 28 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

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TITLE: Current and future aspects of the drug therapy of epilepsy.  
AUTHOR: Tugwell C.  
SOURCE: Hospital Pharmacist, (2003) 10/7 (296-302).

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030 Pharmacology  
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LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB The second article in this month's special feature discusses current anti-epileptic drugs, looks ahead to possible therapeutic developments and emphasises the opportunities for clinical pharmacists to improve medicines management in patients with epilepsy.